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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Kingsbury et al.

Serial No.: To Be Assigned
(Divisional of Serial No. 09/560,639)

Group Art Unit: 1644

Filed: Herewith

Examiner: Roark, J.

For: COMPOSITIONS AND METHODS FOR THE DIAGNOSIS AND TREATMENT OF IMMUNE DISORDERS

Attorney Docket No.: 7853-238

PRELIMINARY AMENDMENT UNDER 37 C.F.R. § 1.115

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In accordance with Rule 115 of the Rules of Practice, please enter the amendments below and consider the remarks below. Applicants submit herewith: (1) a Utility Patent Application Transmittal Cover Sheet; (2) a Divisional Application Transmittal Letter (in duplicate), accompanied by the appropriate provision authorizing payment of the required fee; (3) a copy of the application; (4) a Sequence Listing in paper format; (5) an Information Disclosure Statement (in duplicate), accompanied by the appropriate provision authorizing payment of the required fee; (6) a revised PTO form 1449; (7) Exhibit A, a marked up version of paragraphs in the specification showing the amendments made herein; and (8) Exhibit B, a copy of the pending claims.

It is estimated that no additional fee is required for filing this Amendment. However, should the Patent Office determine otherwise, please charge the necessary fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

IN THE SPECIFICATION:

Please amend the specification as follows:

On page 1, please replace the first paragraph on page 1, lines 8-10 with the following paragraph:

This application is a divisional of U.S. Application No. 09/560,639, filed on April 28, 2000, which claims benefit of provisional Application No. 60/155,862, filed on September 24, 1999, the contents of each of which are incorporated herein by reference in their entirety.

On page 5, please replace the paragraph beginning at line 34 with the following paragraph:

The invention is based, in part, on the discovery of a novel nucleotide sequence depicted in FIG. 8 (SEQ ID NO:12) which encodes a previously unknown human 103 gene product, referred to herein as Athdc120c9 (FIG. 8; SEQ ID NO:13). The invention is also based, in part, on the discovery that the 103 gene is expressed, *in vivo*, in a tightly controlled TH2 or TH2-like specific manner, and that the 103 gene product is an important molecule in signaling TH2-mediated immune responses. In particular, the 103 gene is expressed in a specific subpopulation of T helper cells (*i.e.*, in TH2 or TH2-like cells and not in TH1 or TH1-like cells). For example, results are presented herein which demonstrate that the 103 gene product plays a critical role as a signaling molecule required for the differentiation and function of TH2 and TH2-like cells. In particular, the data presented hereinbelow show that blockage of 103 gene product signaling suppresses both the differentiation and activation of TH2 but not TH1 cell subpopulations. Data are also presented showing that the 103 gene product is a critical regulatory molecule for TH2-mediated immune responses *in vivo*. In particular, results obtained using animal models for allergy and for asthma are presented herein indicating that the 103 gene product provides a critical signal to TH2-mediated responses in these disorders and that blockage of this signal ameliorates symptoms associated with the disorders. For example, the results presented herein in Section 6.4 demonstrate successful amelioration of asthma symptoms by administration of either an anti-103 antibody (*i.e.*, an antibody that specifically binds to a 103 gene product) or a fusion protein comprising an extracellular or secreted domain of a 103 gene product.

On page 144, please replace the abstract with the following abstract:

The present invention relates to methods and compositions for the treatment and diagnosis of immune disorders, especially T helper lymphocyte-related disorders. In

particular, the invention provides a nucleotide sequence which encodes a previously unknown human 103 gene product. The invention also provides expression vectors containing the nucleic acid molecules of the invention and host cells into which the expression vectors have been introduced. The invention still further provides isolated polypeptides, fusion polypeptides, antigenic peptides and antibodies.

IN THE CLAIMS:

Please amend the claims, as follows:

Cancel Claims 1-57, without prejudice.

Add new Claims 58-66, as follows:

58. (new) An isolated polypeptide comprising the amino acid sequence in SEQ ID NO:13.

59. (new) An isolated polypeptide comprising the amino acid sequence encoded by the nucleotide sequence of SEQ ID NO:12.

60. (new) An isolated polypeptide comprising amino acid residues 125 to 158 of SEQ ID NO:13 which is encoded by a nucleic acid molecule which hybridizes to the complement of a nucleic acid molecule that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:13 under hybridization conditions comprising incubation in 6XSSC at 45°C followed by one or more washes in 0.2xSSC/0.1% SDS at 50-65°C.

61. (new) The isolated polypeptide of claim 60, wherein said isolated polypeptide is encoded by a nucleic acid molecule which hybridizes to the complement of the nucleic acid molecule in SEQ ID NO:12 under said hybridization conditions.

62. (new) An isolated polypeptide comprising amino acid residues 125 to 158 of SEQ ID NO:13 which is encoded by a nucleic acid molecule which hybridizes to the complement of a nucleic acid molecule that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:13 under hybridization conditions comprising incubation in 6XSSC at 45°C followed by one or more washes in 0.1xSSC/0.2% SDS at 68°C.

63. (new) The isolated polypeptide of claim 62, wherein said isolated polypeptide is encoded by a nucleic acid molecule which hybridizes to the complement of the nucleic acid molecule in SEQ ID NO:12 under said hybridization conditions.

64. (new) An isolated polypeptide comprising at least amino acid residues:

(a) 125 to 158 of SEQ ID NO:13;

(b) 100 to 158 of SEQ ID NO:13;

(c) 75 to 158 of SEQ ID NO:13;

(d) 50 to 158 of SEQ ID NO:13; or

(e) 25 to 158 of SEQ ID NO:13.

65. (new) The isolated polypeptide of Claim 58, 59, 60, 62 or 64 further comprising a heterologous polypeptide.

66. (new) The isolated polypeptide of Claim 65, wherein the heterologous polypeptide is an Ig polypeptide.

REMARKS

The specification has been amended to correct the claim to priority recited in the specification as originally filed. Specifically, the specification has been amended to indicate that the instant application is a divisional of U.S. Application No. 09/560,639, filed on April 28, 2000, which claims benefit of provisional Application No. 60/155,862, filed on September 24, 1999. The abstract of the application has also been amended to be more descriptive of the claimed invention. A marked up version of the paragraphs in the specification which have been amended, with the deletions and additions to the paragraph indicated by bracketing and underlining, respectively, is attached hereto as Exhibit A. Applicants assert that the amendments to the specification and application do not constitute new subject matter.

Claims 1-57 have been canceled without prejudice to Applicants' right to pursue the subject matter of the canceled claims in subsequent applications. New Claims 58-66 have been added to more particularly point out and distinctly claim the subject matter of the invention. A copy of the pending claims is attached hereto as Exhibit B. Support in the specification for new Claims 58-66 can be found throughout, see, *e.g.*, page 24, line 29 to

page 26, line 16 and page 34, line 21 to page 36, line 21. Applicants assert that no new subject matter has been added with the addition of new Claims 58-66.

Applicants respectfully request entry of the foregoing amendments and remarks into the file history of the above-identified application.

Respectfully submitted,

Date: July 6, 2001

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EXHIBIT A

MARKED UP VERSION OF PARAGRAPHS IN THE SPECIFICATION AS OF JULY 6, 2001 (ATTORNEY DOCKET NO. 7853-238)

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 1, lines 8-10 of the specification:

This application [claims priority under 35 U.S.C. § 119 (e) to U.S. provisional application Serial No. 60/155,862, filed on September 24, 1999, which is incorporated herein, by reference in its entirety] is a divisional of U.S. Application No. 09/560,639, filed on April 28, 2000, which claims benefit of provisional Application No. 60/155,862, filed on September 24, 1999, the contents of each of which are incorporated herein by reference in their entirety.

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 5, line 34 of the specification:

The invention is based, in part, on the discovery of a novel nucleotide sequence depicted in [FIG. 21 (SEQ ID NO:24)] FIG. 8 (SEQ ID NO:12) which encodes a previously unknown human 103 gene product, referred to herein as Athdc120c9 [(FIG. 21; SEQ ID NO:25)] (FIG. 8; SEQ ID NO:13). The invention is also based, in part, on the discovery that the 103 gene is expressed, *in vivo*, in a tightly controlled TH2 or TH2-like specific manner, and that the 103 gene product is an important molecule in signaling TH2-mediated immune responses. In particular, the 103 gene is expressed in a specific subpopulation of T helper cells (*i.e.*, in TH2 or TH2-like cells and not in TH1 or TH1-like cells). For example, results are presented herein which demonstrate that the 103 gene product plays a critical role as a signaling molecule required for the differentiation and function of TH2 and TH2-like cells. In particular, the data presented hereinbelow show that blockage of 103 gene product signaling suppresses both the differentiation and activation of TH2 but not TH1 cell subpopulations. Data are also presented showing that the 103 gene product is a critical regulatory molecule for TH2-mediated immune responses *in vivo*. In particular, results obtained using animal models for allergy and for asthma are presented herein indicating that the 103 gene product provides a critical signal to TH2-mediated responses in these disorders and that blockage of this signal ameliorates symptoms associated with the disorders. For

example, the results presented herein in Section 6.4 demonstrate successful amelioration of asthma symptoms by administration of either an anti-103 antibody (*i.e.*, an antibody that specifically binds to a 103 gene product) or a fusion protein comprising an extracellular or secreted domain of a 103 gene product.

A marked up version of the replacement abstract showing the changes made relative to the abstract on page 144 of the specification:

The present invention relates to methods and compositions for the treatment and diagnosis of immune disorders, especially T helper lymphocyte-related disorders. In particular, the invention provides a novel nucleotide sequence which encodes a previously unknown human 103 gene product. The invention also provides expression vectors containing the nucleic acid molecules of the invention and host cells into which the expression vectors have been introduced. The invention still further provides isolated polypeptides, fusion polypeptides, antigenic peptides and antibodies. [invention describes a gene known in the art, alternatively, as ST2, T1 and Fit-1, and referred to herein as the 103 gene. The 103 gene is disclosed herein to be differentially expressed in TH2 cells and not in TH1 cells. Further, the 103 gene product is demonstrated herein to be an important modulator of TH2 and TH2-like immune response both *in vitro* and *in vivo*. Thus, the 103 gene, its gene products and antibodies that specifically bind thereto can be used diagnostically or as targets for therapeutic intervention in the treatment of a variety of immune disorders.

In this regard, the invention provides methods for the identification and therapeutic use of compounds for treatments of immune disorders, especially TH cell subpopulation-related disorders and including TH2 and TH2-like disorders (*i.e.*, disorders associated with a TH2 or TH2-like mediated immune response) such as atopic conditions (*e.g.*, allergy and asthma). Additionally, methods are provided for the diagnostic evaluation and prognosis of TH cell subpopulation related disorders, for the identification of subjects exhibiting a predisposition to such conditions, for monitoring patients undergoing clinical evaluation for the treatment of such disorders and for monitoring the efficacy of compounds used in clinical trials.]

EXHIBIT B

PENDING CLAIMS AS OF JULY 6, 2001

ATTORNEY DOCKET NO. 7853-238

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58. An isolated polypeptide comprising the amino acid sequence in SEQ ID NO:13.

59. An isolated polypeptide comprising the amino acid sequence encoded by the nucleotide sequence of SEQ ID NO:12.

60. An isolated polypeptide comprising amino acid residues 125 to 158 of SEQ ID NO:13 which is encoded by a nucleic acid molecule which hybridizes to the complement of a nucleic acid molecule that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:13 under hybridization conditions comprising incubation in 6XSSC at 45°C followed by one or more washes in 0.2xSSC/0.1% SDS at 50-65°C.

61. The isolated polypeptide of claim 60, wherein said isolated polypeptide is encoded by a nucleic acid molecule which hybridizes to the complement of the nucleic acid molecule in SEQ ID NO:12 under said hybridization conditions.

62. An isolated polypeptide comprising amino acid residues 125 to 158 of SEQ ID NO:13 which is encoded by a nucleic acid molecule which hybridizes to the complement of a nucleic acid molecule that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:13 under hybridization conditions comprising incubation in 6XSSC at 45°C followed by one or more washes in 0.1xSSC/0.2% SDS at 68°C.

63. The isolated polypeptide of claim 62, wherein said isolated polypeptide is encoded by a nucleic acid molecule which hybridizes to the complement of the nucleic acid molecule in SEQ ID NO:12 under said hybridization conditions.

64. An isolated polypeptide comprising at least amino acid residues:

(a) 125 to 158 of SEQ ID NO:13;

(b) 100 to 158 of SEQ ID NO:13;

(c) 75 to 158 of SEQ ID NO:13;

(d) 50 to 158 of SEQ ID NO:13; or

(e) 25 to 158 of SEQ ID NO:13.

65. The isolated polypeptide of Claim 58, 59, 60, 62 or 64 further comprising a heterologous polypeptide.

66. The isolated polypeptide of Claim 65, wherein the heterologous polypeptide is an Ig polypeptide.